PrevAKI-multicenter-Trial – Intervention
Patient Information Sheet and Informed Consent

Patient Information Sheet

Study site:

Investigator:_____

Institution:_____

Address:_____

Phone number:_____

Biomarker guided implementation of the cardiovascular surgery AKI bundle guidelines to reduce the occurrence of AKI in patients after cardiac surgery (PrevAKI – multicenter-Trial)
– Intervention-
(07-AnIt-16)

DEAR MADAM, DEAR SIR,

we would like to ask you if you are willing to participate in the following clinical trial "Biomarker guided implementation of the cardiovascular surgery AKI bundle guidelines to reduce the occurrence of AKI in patients after cardiac surgery" during your hospital stay.

With this letter, we will inform you about the progress and your further rights within the trial.

The trial is being conducted in several institutions in Europe; a total number of about 310 people are expected to participate. This multicenter trial is initiated, organized and funded by the University Hospital Muenster and the ESICM (European Society of Intensive Care Medicine).

Your participation in this trial is entirely voluntary. You are only included if you declare your consent in writing. Refusal to participate will in no way influence your further care at your institution. You may withdraw your consent and end your participation at any time before or during the trial without stating reasons.

1. Why is this trial conducted?

The main objective of this pilot study is to clarify whether it is possible to implement a bundle of supportive measures (listed below) for protecting the kidneys after cardiac surgery into the clinical routine. Furthermore, it will be investigated whether the occurrence or progress of acute kidney injury (AKI) can be positively influenced by an early use of supportive measures. This clinical trial is designed in order to set up a large international trial aiming to reduce the occurrence of AKI and thus improving the survival of patients after cardiac surgery.
One function of the kidneys is the elimination of metabolic end products, the so-called urinary excreted substances, and toxins from the body by producing urine. Consequently,

the kidneys control fluid balance and regulate the electrolyte and acid-base balance by controlling the composition of the urine. In the context of various diseases, loss of kidney function may occur.
Acute kidney injury is a sudden, within hours to days, occurring, generally reversible impairment of the kidney function. In the context of cardiac surgery with the use of the cardiopulmonary bypass, acute kidney injury is a frequent complication and can occur after normal or already impaired kidney function. Various pre-existing medical conditions as well as possible complications that occur during the treatment e.g. blood poisoning (sepsis), reduced blood volume or drug side effects (e.g. x-ray contrast agents) increase the risk for the development of acute kidney injury.

At present, no clinically established procedure exists that can reduce the occurrence or severity of acute kidney injury after cardiac surgery. However, it has been demonstrated that one specific laboratory parameter indicates at an early stage (approximately 4 hours after surgery) whether patients have an increased risk for the occurrence of acute kidney injury. The objective of the trial is to investigate whether an early onset of supportive measures in high-risk patients can be implemented into the clinical routine. Furthermore, it should be clarified whether this early onset has a positive impact on the occurrence and/or severity of acute kidney injury.

2. What is the trial procedure and what do I have to consider when participating?

In this study, a total of 310 high-risk patients (identified by a routinely determination of a laboratory parameter) will be included after cardiac surgery with cardiopulmonary bypass.
If you are willing to participate in this trial, your medical history will be collected and you will undergo a broad medical examination. Subsequently, assuming your consent, you are randomly assigned to one of the two study groups.

For patients in **the group with early onset of supportive measures**, the following supportive measures are implemented:

- avoidance of all nephrotoxic agents
- Suspend certain drugs (angiotensin converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB)) for 48 hours if clinically possible
- avoidance of hyperglycemia for a total of 72 hours
- Consideration of alternatives to radio contrast agents
- Optimization of blood pressure and fluid status according to specific guidelines based on target variables for 12 hours.

Thereafter, patients receive standard therapy.

Patients in **the control group receive standard therapy** at any time. This means in detail:

- No suspension of ACE-inhibitors
- No additional blood glucose controls as usual on the day of surgery
- The use of contrast agents is not restricted on the day of surgery
- Blood pressure is supported according to the current clinical standard

The physical examinations and medical measures as well as the collection of specific parameters are an integral part of your treatment. Apart from the immediate postoperative treatment (see above), your further medical treatment between the two

study groups does not differ. Only 4 and 12 hours after surgery, 5 mL of urine and 5 mL of blood are taken from an already placed bladder catheter or intravascular catheter. In addition, we will contact you and your family physician 30, 60 and 90 days after your surgery to check your state of health.

IMPORTANT: Participation in the trial will not affect neither the decision-making process of a required therapy nor the standard treatment. You can terminate your participation in this trial at any time, without giving reasons, without having any disadvantages on your medical treatment.

Storage of samples:

The urine and blood samples for the analysis will be stored pseudonymously. Pseudonymously means that only a number and/or letter code (possibly with an indication of the year of birth) are used preventing any conclusions about your name or initials. After the analysis, which will take place in the clinical laboratory of the University Hospital Muenster, the samples are stored for a maximum of 10 years and will be destroyed afterwards.

3. What are the personal benefits of participation in the trial?

If you are assigned into the group with early onset of supporting therapy, this may improve the treatment of your medical condition. However, due to the fact that the advantage for this bundle has not yet been proven, it may also be possible that you do not have the hoped benefit by participation in this trial.
If you are assigned into the group with standard therapy, your prospects of treatment will not differ compared to a non-participation in this trial.
However, the results of this trial may contribute to the improvement of the treatment of patients with increased risk for the development of acute kidney injury.

4. What are the risks associated with the participation in the trial?

By participating in the trial (especially by short-term break of ACE inhibitors and ARBs if clinically possible, avoidance of high blood glucose level, balancing the examination with contrast agents as well as by optimizing blood pressure according to guidelines) you do not have any risk.

The required urine and blood samples for the trial are taken from already placed catheters.

5. Who cannot participate in this trial?

You may not participate in this trial if you are participating in other concurrent trials/clinical research projects or recently have participated (over the past 3 months).

In addition, you may not participate in this trial if you meet one or more of the following criteria:

- Pre-existing acute kidney injury
- Extra-corporeal supporting systems
- Pregnancy, nursing period
- Pre-existing kidney disease, e.g. (Glomerulo-) nephritis, interstitial nephritis or vasculitis
- Chronic renal insufficiency (with eGFR ≤ 20 ml/min)
- Pre-existing renal replacement therapy or condition after acute kidney injury with dialysis dependency
- Kidney transplant within the last 12 months
- Extended relationship with a study team member (e.g. employee, relative, colleague)

The investigator will talk to you in order to clarify further possible exclusion criteria and to answer your questions.

6. Will I incur costs for the participation in the trial?

Your participation in this trial will not incur any additional costs. An expense allowance is not provided.

7. Am I insured during the trial?

During your hospital stay, you are insured according to standard. There is no additional insurance within the trial.

8. Will I am informed of new findings during the clinical trial?

If new findings are gained during the course of the trial that could affect your decision to continue participating in this trial, of course you will be informed immediately. For further information, please contact the investigator.

9. Am I contacted again?

To collect further medical data, we will contact you and your family physician 30, 60 and 90 days after your surgery to check your state of health. If you do not wish to be contacted again, please tick the appropriate box in the declaration of consent.

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10. What happens with my data?

During the trial, medical records and personal information are collected and recorded digitally or in your personal file. The data related to the trial are additionally recorded in a pseudonymized form, analyzed anonymously and, if necessary, passed on.

Pseudonymized means that only a number and/or letter code (possibly with an indication of the year of birth) are used preventing any conclusions about your name or initials.

Only members of the study steam have access to your data. These persons are bound to secrecy. The data are protected against unauthorized access. Decoding only occurs under the conditions prescribed by law.

Scientific publications of results are planned and are performed exclusively anonymously, meaning in a form that does not allow conclusions about your person.

The Data Protection Act contains more detailed guidelines for the required scope of consent to data collection and use. For details, please refer to the declaration of consent, which is attached to this patient information sheet.

13. What happens to my blood and urine samples?

The blood and urine samples are used pseudonymously for the analysis of specific biomarkers to evaluate the progression of disease. Any residual material is stored for 10 years in the Department of Anesthesiology, Intensive Care and Pain Medicine at the University Hospital Muenster.

14. Who can I contact for further questions?

Should you have any questions, please do not hesitate to ask. We will be happy to answer your questions. Please direct your questions to the responsible investigator:

…….. (phone no.: ……..)

or primary care physician.

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Name of Participant/Patient in block letters

Date of birth Patient-ID

I have been informed in a personal talk by the investigator

Name of Investigator

in detail about the nature, importance, risks and scope of the trial. I have also read and understood the text of the information as well as the data protection statement printed below. I had the opportunity to talk with the investigator about the conduct of the trial. All my questions were answered adequately.
In addition to the written patient information the following points were discussed:

I had enough time to decide.

I am aware that I am able to withdraw my consent to participate in the trial (oral or written) at any time, without giving reasons, without incurring any disadvantages for my medical treatment.

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Data protection

I am aware of the fact that personal data, in particular medical findings, should be collected, stored and analyzed within this trial. The use of the data is performed according to legal regulations and requires the following voluntary consent declaration before participation in the clinical trial. This means that without the following consent, I cannot participate in the clinical trial.

1. I agree that personal data, in particular information about my health, will be collected, recorded and stored digitally as well as on paper in the University Hospital Muenster as well as on the electronic platform of the European Society for Intensive Care. If necessary, the collected data are shared in a pseudonymized (coded) form with an office commissioned by the University Hospital Muenster (*sponsor of the study*) for the purpose of scientific evaluation.
2. In addition, I agree that – if necessary for a proper implementation of the trial - authorized and confidential commissioners of the sponsor, as well as the responsible supervisory authorities, get insight to my personal data, particularly my health data (available at the investigator). For this purpose I discharge the investigator from medical confidentiality.
3. I agree that my data will be stored for at least ten years after the termination or discontinuation of the trial, as determined by the rules on the trial of pharmaceuticals. All my personal data will be deleted afterwards, unless no statutory retention periods exist.
5. I am informed of the following legal regulations: If I withdraw my consent to participate in the trial, the collected data will be deleted and blood and urine samples will be destroyed at my request.
6. I agree that health data are collected or viewed by co-treating physicians if this is necessary for the proper conduct and monitoring of the trial. For this purpose I discharge these physicians from medical confidentiality.
7. I agree that my family physician

   .....
   Name

   is informed about my participation in the clinical trial.

I freely give my consent to participate in the PrevAKI-multicenter-Trial.

I received a copy of the patient information sheet and consent. One copy remains in the study center.

.....
Name of Participant/Patient in block letters

_____ _____ _____
Date Time Signature of Participant/Patient

I conducted the informed consent discussion and obtained the consent of the patient.

.....
Name of Investigator in block letters

_____ _____
Date Signature of Investigator